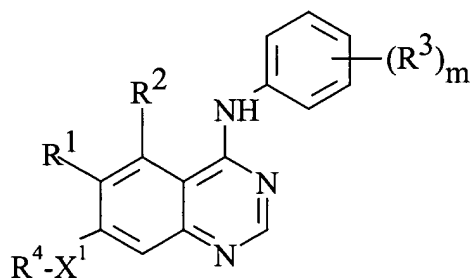


**IN THE CLAIMS:**

Claims 1-16 (canceled).

Claim 17 (previously presented): A method for producing an anti-cancer effect in a warm-blooded animal in need of such treatment which comprises administering to said animal an effective amount of a quinazoline derivative of formula I:



(I)

wherein:

m is an integer from 1 to 2;

R<sup>1</sup> represents hydrogen, hydroxy, halogeno, nitro, trifluoromethyl, cyano, C<sub>1-3</sub>alkyl, C<sub>1-3</sub>alkoxy, C<sub>1-3</sub>alkylthio, or -NR<sup>5</sup>R<sup>6</sup> (wherein R<sup>5</sup> and R<sup>6</sup>, which may be the same or different, each represents hydrogen or C<sub>1-3</sub>alkyl);

R<sup>2</sup> represents hydrogen, hydroxy, halogeno, methoxy, amino or nitro;

R<sup>3</sup> represents hydroxy, halogeno, C<sub>1-3</sub>alkyl, C<sub>1-3</sub>alkoxy, C<sub>1-3</sub>alkanoyloxy, trifluoromethyl, cyano, amino or nitro;

X<sup>1</sup> represents -CH<sub>2</sub>-, -S-, -SO-, -SO<sub>2</sub>-, -NR<sup>7</sup>CO-, -CONR<sup>8</sup>-, -SO<sub>2</sub>NR<sup>9</sup>-, -NR<sup>10</sup>SO<sub>2</sub>- or -NR<sup>11</sup>- (wherein R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup> and R<sup>11</sup> each independently represents hydrogen, C<sub>1-3</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl);

R<sup>4</sup> is selected from one of the following twelve groups:

- 1) C<sub>1-5</sub>alkylR<sup>12</sup> (wherein R<sup>12</sup> is a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which heterocyclic group is linked to C<sub>1-5</sub>alkyl through a carbon atom and which heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C<sub>1-4</sub>alkyl,

C<sub>1-4</sub>hydroxyalkyl, C<sub>1-4</sub>alkoxy, carbamoyl, C<sub>1-4</sub>alkylcarbamoyl, N,N-di(C<sub>1-4</sub>alkyl)carbamoyl, C<sub>1-4</sub>alkanoyl and C<sub>1-4</sub>alkoxycarbonyl) or C<sub>1-5</sub>alkylR<sup>13</sup> (wherein R<sup>13</sup> is a group selected from pyrrolidin-1-yl, imidazolidin-1-yl and thiomorpholino, which group may bear one or two substituents selected from oxo, hydroxy, halogeno, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, C<sub>1-4</sub>alkoxy, carbamoyl, C<sub>1-4</sub>alkylcarbamoyl, N,N-di(C<sub>1-4</sub>alkyl)carbamoyl, C<sub>1-4</sub>alkanoyl and C<sub>1-4</sub>alkoxycarbonyl);

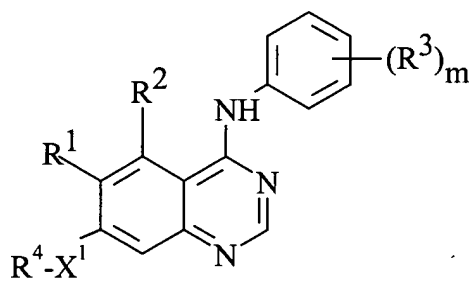
- 2) C<sub>2-5</sub>alkenylR<sup>14</sup> (wherein R<sup>14</sup> is a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, C<sub>1-4</sub>alkoxy, carbamoyl, C<sub>1-4</sub>alkylcarbamoyl, N,N-di(C<sub>1-4</sub>alkyl)carbamoyl, C<sub>1-4</sub>alkanoyl and C<sub>1-4</sub>alkoxycarbonyl);
- 3) C<sub>2-5</sub>alkynylR<sup>15</sup> (wherein R<sup>15</sup> is a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, C<sub>1-4</sub>alkoxy, carbamoyl, C<sub>1-4</sub>alkylcarbamoyl, N,N-di(C<sub>1-4</sub>alkyl)carbamoyl, C<sub>1-4</sub>alkanoyl and C<sub>1-4</sub>alkoxycarbonyl);
- 4) C<sub>1-5</sub>alkylX<sup>2</sup>C<sub>1-5</sub>alkylX<sup>3</sup>R<sup>16</sup> (wherein X<sup>2</sup> and X<sup>3</sup> which may be the same or different are each -O-, -S-, -SO-, -SO<sub>2</sub>-, -NR<sup>17</sup>CO-, -CONR<sup>18</sup>-, -SO<sub>2</sub>NR<sup>19</sup>-, -NR<sup>20</sup>SO<sub>2</sub>- or -NR<sup>21</sup>- (wherein R<sup>17</sup>, R<sup>18</sup>, R<sup>19</sup>, R<sup>20</sup> and R<sup>21</sup> each independently represents hydrogen, C<sub>1-3</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl) and R<sup>16</sup> represents hydrogen or C<sub>1-3</sub>alkyl) with the proviso that X<sup>1</sup> cannot be -CH<sub>2</sub>- when R<sup>4</sup> is C<sub>1-5</sub>alkylX<sup>2</sup>C<sub>1-5</sub>alkylX<sup>3</sup>R<sup>16</sup>;
- 5) C<sub>1-5</sub>alkylX<sup>4</sup>COR<sup>22</sup> (wherein X<sup>4</sup> represents -O- or -NR<sup>23</sup>- (wherein R<sup>23</sup> represents hydrogen, C<sub>1-3</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl) and R<sup>22</sup> represents -NR<sup>24</sup>R<sup>25</sup> or -OR<sup>26</sup> (wherein R<sup>24</sup>, R<sup>25</sup> and R<sup>26</sup> which may be the same or different each represents hydrogen, C<sub>1-4</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl));
- 6) C<sub>1-5</sub>alkylX<sup>5</sup>R<sup>27</sup> (wherein X<sup>5</sup> represents -O-, -S-, -SO-, -SO<sub>2</sub>-, -OCO-, -NR<sup>28</sup>CO-, -CONR<sup>29</sup>-, -SO<sub>2</sub>NR<sup>30</sup>-, -NR<sup>31</sup>SO<sub>2</sub>- or -NR<sup>32</sup>- (wherein R<sup>28</sup>, R<sup>29</sup>, R<sup>30</sup>, R<sup>31</sup> and R<sup>32</sup> each independently represents hydrogen, C<sub>1-3</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl) or X<sup>5</sup> is carbonyl, and R<sup>27</sup> represents cyclopentyl, cyclohexyl or a 5 or 6 membered saturated

heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which cyclopentyl, cyclohexyl or heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, C<sub>1-4</sub>alkoxy, carbamoyl, C<sub>1-4</sub>alkylcarbamoyl, N,N-di(C<sub>1-4</sub>alkyl)carbamoyl, C<sub>1-4</sub>alkanoyl and C<sub>1-4</sub>alkoxycarbonyl or R<sup>27</sup> is C<sub>1-3</sub>alkyl with the proviso that when R<sup>27</sup> is C<sub>1-3</sub>alkyl, X<sup>5</sup> is -S-, -SO-, -SO<sub>2</sub>-, -SO<sub>2</sub>NR<sup>30</sup>- or -NR<sup>31</sup>SO<sub>2</sub>- and X<sup>1</sup> is not -CH<sub>2</sub>-);

- 7) C<sub>1-3</sub>alkoxyC<sub>2-4</sub>alkyl provided that X<sup>1</sup> is -S-, -SO- or -SO<sub>2</sub>-;
- 8) C<sub>1-5</sub>alkylX<sup>6</sup>C<sub>1-5</sub>alkylR<sup>33</sup> (wherein X<sup>6</sup> represents -O-, -S-, -SO-, -SO<sub>2</sub>-, -NR<sup>34</sup>CO-, -CONR<sup>35</sup>-, -SO<sub>2</sub>NR<sup>36</sup>-, -NR<sup>37</sup>SO<sub>2</sub>- or -NR<sup>38</sup>- (wherein R<sup>34</sup>, R<sup>35</sup>, R<sup>36</sup>, R<sup>37</sup> and R<sup>38</sup> each independently represents hydrogen, C<sub>1-3</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl) and R<sup>33</sup> represents cyclopentyl, cyclohexyl or a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which cyclopentyl, cyclohexyl or heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, C<sub>1-4</sub>alkoxy, carbamoyl, C<sub>1-4</sub>alkylcarbamoyl, N,N-di(C<sub>1-4</sub>alkyl)carbamoyl, C<sub>1-4</sub>alkanoyl and C<sub>1-4</sub>alkoxycarbonyl);
- 9) R<sup>39</sup> (wherein R<sup>39</sup> is a group selected from pyrrolidin-3-yl, piperidin-3-yl and piperidin-4-yl which group may bear one or two substituents selected from oxo, hydroxy, halogeno, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, C<sub>1-4</sub>alkoxy, carbamoyl, C<sub>1-4</sub>alkylcarbamoyl, N,N-di(C<sub>1-4</sub>alkyl)carbamoyl, C<sub>1-4</sub>alkanoyl and C<sub>1-4</sub>alkoxycarbonyl);
- 10) C<sub>1-5</sub>alkylR<sup>40</sup> (wherein R<sup>40</sup> is piperazin-1-yl which bears at least one substituent selected from C<sub>1-4</sub>alkanoyl, C<sub>1-4</sub>alkoxycarbonyl, C<sub>1-4</sub>hydroxyalkyl and -CONR<sup>41</sup>R<sup>42</sup> (wherein R<sup>41</sup> and R<sup>42</sup> each independently represents hydrogen or C<sub>1-4</sub>alkyl);
- 11) C<sub>1-5</sub>alkylR<sup>43</sup> (wherein R<sup>43</sup> is morpholino which may bear one or two substituents selected from oxo, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, carbamoyl, C<sub>1-4</sub>alkylcarbamoyl, N,N-di(C<sub>1-4</sub>alkyl)carbamoyl, C<sub>1-4</sub>alkanoyl and C<sub>1-4</sub>alkoxycarbonyl) with the proviso that when R<sup>4</sup> is C<sub>1-5</sub>alkylR<sup>43</sup>, X<sup>1</sup> is -S-, -SO-, -SO<sub>2</sub>-, -SO<sub>2</sub>NR<sup>9</sup>- or -NR<sup>10</sup>SO<sub>2</sub>-; and

12) C<sub>1-5</sub>alkylR<sup>44</sup> (wherein R<sup>44</sup> is morpholino which bears at least one and optionally two substituents selected from oxo, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, carbamoyl, C<sub>1-4</sub>alkylcarbamoyl, N,N-di(C<sub>1-4</sub>alkyl)carbamoyl, C<sub>1-4</sub>alkanoyl and C<sub>1-4</sub>alkoxycarbonyl);  
or a pharmaceutically acceptable salt thereof.

Claim 18 (currently amended): A method for inhibiting the effects of VEGF in a warm-blooded animal in need of such treatment which comprises administering to said animal an effective inhibiting amount of a quinazoline derivative of formula I:



(I)

wherein:

m is an integer from 1 to 2;

R<sup>1</sup> represents hydrogen, hydroxy, halogeno, nitro, trifluoromethyl, cyano, C<sub>1-3</sub>alkyl, C<sub>1-3</sub>alkoxy, C<sub>1-3</sub>alkylthio, or -NR<sup>5</sup>R<sup>6</sup> (wherein R<sup>5</sup> and R<sup>6</sup>, which may be the same or different, each represents hydrogen or C<sub>1-3</sub>alkyl);

R<sup>2</sup> represents hydrogen, hydroxy, halogeno, methoxy, amino or nitro;

R<sup>3</sup> represents hydroxy, halogeno, C<sub>1-3</sub>alkyl, C<sub>1-3</sub>alkoxy, C<sub>1-3</sub>alkanoyloxy, trifluoromethyl, cyano, amino or nitro;

X<sup>1</sup> represents -CH<sub>2</sub>-, -S-, -SO-, -SO<sub>2</sub>-, -NR<sup>7</sup>CO-, -CONR<sup>8</sup>-, -SO<sub>2</sub>NR<sup>9</sup>-, -NR<sup>10</sup>SO<sub>2</sub>- or -NR<sup>11</sup>- (wherein R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup> and R<sup>11</sup> each independently represents hydrogen, C<sub>1-3</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl);

R<sup>4</sup> is selected from one of the following twelve groups:

- 1) C<sub>1-5</sub>alkylR<sup>12</sup> (wherein R<sup>12</sup> is a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which heterocyclic group is linked to C<sub>1-5</sub>alkyl through a carbon atom and which heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, C<sub>1-4</sub>alkoxy, carbamoyl, C<sub>1-4</sub>alkylcarbamoyl, N,N-di(C<sub>1-4</sub>alkyl)carbamoyl, C<sub>1-4</sub>alkanoyl and C<sub>1-4</sub>alkoxycarbonyl) or C<sub>1-5</sub>alkylR<sup>13</sup> (wherein R<sup>13</sup> is a group selected from pyrrolidin-1-yl, imidazolidin-1-yl and thiomorpholino, which group may bear one or two substituents selected from oxo, hydroxy, halogeno, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, C<sub>1-4</sub>alkoxy, carbamoyl, C<sub>1-4</sub>alkylcarbamoyl, N,N-di(C<sub>1-4</sub>alkyl)carbamoyl, C<sub>1-4</sub>alkanoyl and C<sub>1-4</sub>alkoxycarbonyl);
- 2) C<sub>2-5</sub>alkenylR<sup>14</sup> (wherein R<sup>14</sup> is a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, C<sub>1-4</sub>alkoxy, carbamoyl, C<sub>1-4</sub>alkylcarbamoyl, N,N-di(C<sub>1-4</sub>alkyl)carbamoyl, C<sub>1-4</sub>alkanoyl and C<sub>1-4</sub>alkoxycarbonyl);
- 3) C<sub>2-5</sub>alkynylR<sup>15</sup> (wherein R<sup>15</sup> is a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, C<sub>1-4</sub>alkoxy, carbamoyl, C<sub>1-4</sub>alkylcarbamoyl, N,N-di(C<sub>1-4</sub>alkyl)carbamoyl, C<sub>1-4</sub>alkanoyl and C<sub>1-4</sub>alkoxycarbonyl);
- 4) C<sub>1-5</sub>alkylX<sup>2</sup>C<sub>1-5</sub>alkylX<sup>3</sup>R<sup>16</sup> (wherein X<sup>2</sup> and X<sup>3</sup> which may be the same or different are each -O-, -S-, -SO-, -SO<sub>2</sub>-, -NR<sup>17</sup>CO-, -CONR<sup>18</sup>-, -SO<sub>2</sub>NR<sup>19</sup>-, -NR<sup>20</sup>SO<sub>2</sub>- or -NR<sup>21</sup>- (wherein R<sup>17</sup>, R<sup>18</sup>, R<sup>19</sup>, R<sup>20</sup> and R<sup>21</sup> each independently represents hydrogen, C<sub>1-3</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl) and R<sup>16</sup> represents hydrogen or C<sub>1-3</sub>alkyl) with the proviso that X<sup>1</sup> cannot be -CH<sub>2</sub>- when R<sup>4</sup> is C<sub>1-5</sub>alkylX<sup>2</sup>C<sub>1-5</sub>alkylX<sup>3</sup>R<sup>16</sup>;
- 5) C<sub>1-5</sub>alkylX<sup>4</sup>COR<sup>22</sup> (wherein X<sup>4</sup> represents -O- or -NR<sup>23</sup>- (wherein R<sup>23</sup> represents hydrogen, C<sub>1-3</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl) and R<sup>22</sup> represents -NR<sup>24</sup>R<sup>25</sup> or -OR<sup>26</sup>

(wherein R<sup>24</sup>, R<sup>25</sup> and R<sup>26</sup> which may be the same or different each represents hydrogen, C<sub>1-4</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl));

6) C<sub>1-5</sub>alkylX<sup>5</sup>R<sup>27</sup> (wherein X<sup>5</sup> represents -O-, -S-, -SO-, -SO<sub>2</sub>-, -OCO-, -NR<sup>28</sup>CO-, -CONR<sup>29</sup>-, -SO<sub>2</sub>NR<sup>30</sup>-, -NR<sup>31</sup>SO<sub>2</sub>- or -NR<sup>32</sup>- (wherein R<sup>28</sup>, R<sup>29</sup>, R<sup>30</sup>, R<sup>31</sup> and R<sup>32</sup> each independently represents hydrogen, C<sub>1-3</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl) or X<sup>5</sup> is carbonyl, and R<sup>27</sup> represents cyclopentyl, cyclohexyl or a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which cyclopentyl, cyclohexyl or heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, C<sub>1-4</sub>alkoxy, carbamoyl, C<sub>1-4</sub>alkylcarbamoyl, N,N-di(C<sub>1-4</sub>alkyl)carbamoyl, C<sub>1-4</sub>alkanoyl and C<sub>1-4</sub>alkoxycarbonyl or R<sup>27</sup> is C<sub>1-3</sub>alkyl with the proviso that when R<sup>27</sup> is C<sub>1-3</sub>alkyl, X<sup>5</sup> is -S-, -SO-, -SO<sub>2</sub>-, -SO<sub>2</sub>NR<sup>30</sup>- or -NR<sup>31</sup>SO<sub>2</sub>- and X<sup>1</sup> is not -CH<sub>2</sub>-);

7) C<sub>1-3</sub>alkoxyC<sub>2-4</sub>alkyl provided that X<sup>1</sup> is -S-, -SO- or -SO<sub>2</sub>-;

8) C<sub>1-5</sub>alkylX<sup>6</sup>C<sub>1-5</sub>alkylR<sup>33</sup> (wherein X<sup>6</sup> represents -O-, -S-, -SO-, -SO<sub>2</sub>-, -NR<sup>34</sup>CO-, -CONR<sup>35</sup>-, -SO<sub>2</sub>NR<sup>36</sup>-, -NR<sup>37</sup>SO<sub>2</sub>- or -NR<sup>38</sup>- (wherein R<sup>34</sup>, R<sup>35</sup>, R<sup>36</sup>, R<sup>37</sup> and R<sup>38</sup> each independently represents hydrogen, C<sub>1-3</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl) and R<sup>33</sup> represents cyclopentyl, cyclohexyl or a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which cyclopentyl, cyclohexyl or heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, C<sub>1-4</sub>alkoxy, carbamoyl, C<sub>1-4</sub>alkylcarbamoyl, N,N-di(C<sub>1-4</sub>alkyl)carbamoyl, C<sub>1-4</sub>alkanoyl and C<sub>1-4</sub>alkoxycarbonyl);

9) R<sup>39</sup> (wherein R<sup>39</sup> is a group selected from pyrrolidin-3-yl, piperidin-3-yl and piperidin-4-yl which group may bear one or two substituents selected from oxo, hydroxy, halogeno, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, C<sub>1-4</sub>alkoxy, carbamoyl, C<sub>1-4</sub>alkylcarbamoyl, N,N-di(C<sub>1-4</sub>alkyl)carbamoyl, C<sub>1-4</sub>alkanoyl and C<sub>1-4</sub>alkoxycarbonyl);

10) C<sub>1-5</sub>alkylR<sup>40</sup> (wherein R<sup>40</sup> is piperazin-1-yl which bears at least one substituent selected from C<sub>1-4</sub>alkanoyl, C<sub>1-4</sub>alkoxycarbonyl, C<sub>1-4</sub>hydroxyalkyl and -CONR<sup>41</sup>R<sup>42</sup>

(wherein R<sup>41</sup> and R<sup>42</sup> each independently represents hydrogen or C<sub>1-4</sub>alkyl);

11) C<sub>1-5</sub>alkylR<sup>43</sup> (wherein R<sup>43</sup> is morpholino which may bear one or two substituents selected from oxo, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, carbamoyl, C<sub>1-4</sub>alkylcarbamoyl,

N,N-di(C<sub>1-4</sub>alkyl)carbamoyl, C<sub>1-4</sub>alkanoyl and C<sub>1-4</sub>alkoxycarbonyl) with the proviso

that when R<sup>4</sup> is C<sub>1-5</sub>alkylR<sup>43</sup>, X<sup>1</sup> is -S-, -SO-, -SO<sub>2</sub>-, -SO<sub>2</sub>NR<sup>9</sup>- or -NR<sup>10</sup>SO<sub>2</sub>-; and

12) C<sub>1-5</sub>alkylR<sup>44</sup> (wherein R<sup>44</sup> is morpholino which bears at least one and optionally two substituents selected from oxo, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, carbamoyl,

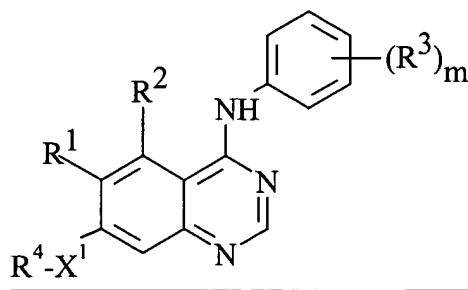
C<sub>1-4</sub>alkylcarbamoyl, N,N-di(C<sub>1-4</sub>alkyl)carbamoyl, C<sub>1-4</sub>alkanoyl and

C<sub>1-4</sub>alkoxycarbonyl);

or a pharmaceutically acceptable salt thereof. ~~or a pharmaceutically salt thereof.~~

Claim 19 (previously presented): A method for inhibiting the effects of VEGF and EGF in a warm-blooded animal in need of such treatment which comprises administering to said animal an effective inhibiting amount of a quinazoline derivative of formula I as claimed in claim 18 or a pharmaceutically acceptable salt thereof.

Claim 20 (currently amended): A method for inhibiting the growth of a solid tumour of the colon, breast, prostate, lung or skin in a warm-blooded animal in need of such treatment which comprises administering to said animal an effective inhibiting amount of a quinazoline derivative of formula I;



wherein:

m is an integer from 1 to 2;

R<sup>1</sup> represents hydrogen, hydroxy, halogeno, nitro, trifluoromethyl, cyano, C<sub>1-3</sub>alkyl, C<sub>1-3</sub>alkoxy, C<sub>1-3</sub>alkylthio, or -NR<sup>5</sup>R<sup>6</sup> (wherein R<sup>5</sup> and R<sup>6</sup>, which may be the same or different, each represents hydrogen or C<sub>1-3</sub>alkyl);

R<sup>2</sup> represents hydrogen, hydroxy, halogeno, methoxy, amino or nitro;

R<sup>3</sup> represents hydroxy, halogeno, C<sub>1-3</sub>alkyl, C<sub>1-3</sub>alkoxy, C<sub>1-3</sub>alkanoyloxy, trifluoromethyl, cyano, amino or nitro;

X<sup>1</sup> represents -CH<sub>2</sub>-, -S-, -SO-, -SO<sub>2</sub>-, -NR<sup>7</sup>CO-, -CONR<sup>8</sup>-, -SO<sub>2</sub>NR<sup>9</sup>-, -NR<sup>10</sup>SO<sub>2</sub>- or -NR<sup>11</sup>- (wherein R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup> and R<sup>11</sup> each independently represents hydrogen, C<sub>1-3</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl);

R<sup>4</sup> is selected from one of the following twelve groups:

- 1) C<sub>1-5</sub>alkylR<sup>12</sup> (wherein R<sup>12</sup> is a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which heterocyclic group is linked to C<sub>1-5</sub>alkyl through a carbon atom and which heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, C<sub>1-4</sub>alkoxy, carbamoyl, C<sub>1-4</sub>alkylcarbamoyl, N,N-di(C<sub>1-4</sub>alkyl)carbamoyl, C<sub>1-4</sub>alkanoyl and C<sub>1-4</sub>alkoxycarbonyl) or C<sub>1-5</sub>alkylR<sup>13</sup> (wherein R<sup>13</sup> is a group selected from pyrrolidin-1-yl, imidazolidin-1-yl and thiomorpholino, which group may bear one or two substituents selected from oxo, hydroxy, halogeno, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, C<sub>1-4</sub>alkoxy, carbamoyl,



C<sub>1-4</sub>alkylcarbamoyl, N,N-di(C<sub>1-4</sub>alkyl)carbamoyl, C<sub>1-4</sub>alkanoyl and C<sub>1-4</sub>alkoxycarbonyl);

- 2) C<sub>2-5</sub>alkenylR<sup>14</sup> (wherein R<sup>14</sup> is a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, C<sub>1-4</sub>alkoxy, carbamoyl, C<sub>1-4</sub>alkylcarbamoyl, N,N-di(C<sub>1-4</sub>alkyl)carbamoyl, C<sub>1-4</sub>alkanoyl and C<sub>1-4</sub>alkoxycarbonyl);
- 3) C<sub>2-5</sub>alkynylR<sup>15</sup> (wherein R<sup>15</sup> is a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, C<sub>1-4</sub>alkoxy, carbamoyl, C<sub>1-4</sub>alkylcarbamoyl, N,N-di(C<sub>1-4</sub>alkyl)carbamoyl, C<sub>1-4</sub>alkanoyl and C<sub>1-4</sub>alkoxycarbonyl);
- 4) C<sub>1-5</sub>alkylX<sup>2</sup>C<sub>1-5</sub>alkylX<sup>3</sup>R<sup>16</sup> (wherein X<sup>2</sup> and X<sup>3</sup> which may be the same or different are each -O-, -S-, -SO-, -SO<sub>2</sub>-, -NR<sup>17</sup>CO-, -CONR<sup>18</sup>-, -SO<sub>2</sub>NR<sup>19</sup>-, -NR<sup>20</sup>SO<sub>2</sub>- or -NR<sup>21</sup>- (wherein R<sup>17</sup>, R<sup>18</sup>, R<sup>19</sup>, R<sup>20</sup> and R<sup>21</sup> each independently represents hydrogen, C<sub>1-3</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl) and R<sup>16</sup> represents hydrogen or C<sub>1-3</sub>alkyl) with the proviso that X<sup>1</sup> cannot be -CH<sub>2</sub>- when R<sup>4</sup> is C<sub>1-5</sub>alkylX<sup>2</sup>C<sub>1-5</sub>alkylX<sup>3</sup>R<sup>16</sup>;
- 5) C<sub>1-5</sub>alkylX<sup>4</sup>COR<sup>22</sup> (wherein X<sup>4</sup> represents -O- or -NR<sup>23</sup>- (wherein R<sup>23</sup> represents hydrogen, C<sub>1-3</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl) and R<sup>22</sup> represents -NR<sup>24</sup>R<sup>25</sup> or -OR<sup>26</sup> (wherein R<sup>24</sup>, R<sup>25</sup> and R<sup>26</sup> which may be the same or different each represents hydrogen, C<sub>1-4</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl));
- 6) C<sub>1-5</sub>alkylX<sup>5</sup>R<sup>27</sup> (wherein X<sup>5</sup> represents -O-, -S-, -SO-, -SO<sub>2</sub>-, -OCO-, -NR<sup>28</sup>CO-, -CONR<sup>29</sup>-, -SO<sub>2</sub>NR<sup>30</sup>-, -NR<sup>31</sup>SO<sub>2</sub>- or -NR<sup>32</sup>- (wherein R<sup>28</sup>, R<sup>29</sup>, R<sup>30</sup>, R<sup>31</sup> and R<sup>32</sup> each independently represents hydrogen, C<sub>1-3</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl) or X<sup>5</sup> is carbonyl, and R<sup>27</sup> represents cyclopentyl, cyclohexyl or a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which cyclopentyl, cyclohexyl or heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, C<sub>1-4</sub>alkoxy, carbamoyl, C<sub>1-4</sub>alkylcarbamoyl, N,N-di(C<sub>1-4</sub>alkyl)carbamoyl, C<sub>1-4</sub>alkanoyl and C<sub>1-4</sub>alkoxycarbonyl or R<sup>27</sup> is C<sub>1-3</sub>alkyl with the proviso that when

R<sup>27</sup> is C<sub>1-3</sub>alkyl, X<sup>5</sup> is -S-, -SO-, -SO<sub>2</sub>-, -SO<sub>2</sub>NR<sup>30</sup>- or -NR<sup>31</sup>SO<sub>2</sub>- and X<sup>1</sup> is not -CH<sub>2</sub>-;

7) C<sub>1-3</sub>alkoxyC<sub>2-4</sub>alkyl provided that X<sup>1</sup> is -S-, -SO- or -SO<sub>2</sub>-;

8) C<sub>1-5</sub>alkylX<sup>6</sup>C<sub>1-5</sub>alkylR<sup>33</sup> (wherein X<sup>6</sup> represents -O-, -S-, -SO-, -SO<sub>2</sub>-, -NR<sup>34</sup>CO-, -CONR<sup>35</sup>-, -SO<sub>2</sub>NR<sup>36</sup>-, -NR<sup>37</sup>SO<sub>2</sub>- or -NR<sup>38</sup>- (wherein R<sup>34</sup>, R<sup>35</sup>, R<sup>36</sup>, R<sup>37</sup> and R<sup>38</sup> each independently represents hydrogen, C<sub>1-3</sub>alkyl or C<sub>1-3</sub>alkoxyC<sub>2-3</sub>alkyl) and R<sup>33</sup> represents cyclopentyl, cyclohexyl or a 5 or 6 membered saturated heterocyclic group with one or two heteroatoms, selected independently from O, S and N, which cyclopentyl, cyclohexyl or heterocyclic group may bear one or two substituents selected from oxo, hydroxy, halogeno, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, C<sub>1-4</sub>alkoxy, carbamoyl, C<sub>1-4</sub>alkylcarbamoyl, N,N-di(C<sub>1-4</sub>alkyl)carbamoyl, C<sub>1-4</sub>alkanoyl and C<sub>1-4</sub>alkoxycarbonyl);

9) R<sup>39</sup> (wherein R<sup>39</sup> is a group selected from pyrrolidin-3-yl, piperidin-3-yl and piperidin-4-yl which group may bear one or two substituents selected from oxo, hydroxy, halogeno, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, C<sub>1-4</sub>alkoxy, carbamoyl, C<sub>1-4</sub>alkylcarbamoyl, N,N-di(C<sub>1-4</sub>alkyl)carbamoyl, C<sub>1-4</sub>alkanoyl and C<sub>1-4</sub>alkoxycarbonyl);

10) C<sub>1-5</sub>alkylR<sup>40</sup> (wherein R<sup>40</sup> is piperazin-1-yl which bears at least one substituent selected from C<sub>1-4</sub>alkanoyl, C<sub>1-4</sub>alkoxycarbonyl, C<sub>1-4</sub>hydroxyalkyl and -CONR<sup>41</sup>R<sup>42</sup> (wherein R<sup>41</sup> and R<sup>42</sup> each independently represents hydrogen or C<sub>1-4</sub>alkyl);

11) C<sub>1-5</sub>alkylR<sup>43</sup> (wherein R<sup>43</sup> is morpholino which may bear one or two substituents selected from oxo, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, carbamoyl, C<sub>1-4</sub>alkylcarbamoyl, N,N-di(C<sub>1-4</sub>alkyl)carbamoyl, C<sub>1-4</sub>alkanoyl and C<sub>1-4</sub>alkoxycarbonyl) with the proviso that when R<sup>4</sup> is C<sub>1-5</sub>alkylR<sup>43</sup>, X<sup>1</sup> is -S-, -SO-, -SO<sub>2</sub>-, -SO<sub>2</sub>NR<sup>9</sup>- or -NR<sup>10</sup>SO<sub>2</sub>-; and

12) C<sub>1-5</sub>alkylR<sup>44</sup> (wherein R<sup>44</sup> is morpholino which bears at least one and optionally two substituents selected from oxo, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>hydroxyalkyl, carbamoyl, C<sub>1-4</sub>alkylcarbamoyl, N,N-di(C<sub>1-4</sub>alkyl)carbamoyl, C<sub>1-4</sub>alkanoyl and C<sub>1-4</sub>alkoxycarbonyl);

or a pharmaceutically acceptable salt thereof. ~~or a pharmaceutically acceptable salt thereof.~~

Claim 21 (previously presented): The method according to claim 20 wherein the tumour is of the colon.

Claim 22 (previously presented): The method according to claim 20 wherein the tumour is of the lung.